

What is claimed is:

Sub A 1

1. A method for treating a vascular graft comprising,
a) introducing into susceptible cells of the graft an effective amount of at least one nucleic acid encoding at least one agent that increases activated protein C (APC) in the graft,
b) expressing the agent in the cells; and
c) increasing the APC sufficient to treat the graft.

10 2. The method of claim 1, wherein at least step a) of the method is performed
ex vivo.

15 3. The method of claim 1, wherein the method further comprises transplanting the treated graft into a host.

20 4. The method of claim 1, wherein prior to step a) of the method, the graft is transplanted into a host.

5. The method of claim 1, wherein the method is performed on the vascular graft *in vivo.*

25 6. The method of claim 3, wherein the transplanted vascular graft has sufficient APC to prevent or treat early or late graft failure as determined by a standard protein C assay.

Sub A 2

7. The method of 6, wherein the graft exhibits at least about a 10% decrease in accelerated atherosclerosis as determined by the standard atherosclerotic vein graft model.

8. The method of claim 6 or 7, wherein the protein C level of the treated graft is at least about one order of magnitude higher than a control vessel as determined by the standard protein C detection assay.

5 9. The method of claim 6 or 7, wherein the increased protein C level of the treated vascular graft is detectable for at least about a week.

10 10. The method of claim 8, wherein the increased protein C level of the treated vascular graft is detectable for at least about a week.

11. The method of claim 6, wherein the early graft failure is accompanied by thrombosis.

12. The method of claim 6, wherein the late graft failure is accompanied by neointimal hyperplasia.

13. The method of claim 1, wherein at least one of the agents is human thrombomodulin (TM), human endothelial protein C receptor (EPCR), human I_KB factor; or a functional fragment thereof.

14. The method of claim 1, wherein the nucleic acid is inserted into a cassette.

15. The method of claim 14, wherein the cassette includes a promoter.

25 16. The method of claim 15, wherein the cassette is inserted into a vector.

17. The method of claim 16, wherein the vector comprises sequence from an adenovirus, retrovirus, or adeno-associated virus.

30 18. The method of claim 17, wherein the vector is a replication defective adenovirus.

19. The method of claim 1, wherein the nucleic acid encodes at least one other anticoagulant molecule.

5 20. The method of claim 19, wherein the anticoagulant molecule is human thrombomodulin or a functional fragment thereof.

10 21. The method of claim 3, wherein the host is susceptible to an inflammatory or immunological stimulus and the method further comprises administering a therapeutic amount of at least one anti-coagulant, antithrombotic, or thrombolytic drug to treat or prevent that stimulus.

22. The method of claim 21, wherein the drug is administered before step a) or after step c) of the method.

23. The method of claim 22, wherein the anti-coagulant drug is coumadin.

24. A method for engineering a vascular graft that resists failure, the method comprising:

a) introducing into susceptible cells of the graft an effective amount of at least one nucleic acid encoding at least one agent that increases activated protein C (APC) in the graft;

b) expressing the agent in the cells; and

c) increasing the APC in the graft sufficient to resist graft failure.

25 25. An engineered vascular graft produced by the method of claim 24.

26. The vascular graft of claim 25, wherein the graft is an autologous saphenous vein graft (SVG) or an artificial graft.

27. The engineered vascular graft of claim 25, wherein the graft is an arterial graft.

28. A kit for performing the methods of claims 1 or 24, the kit comprising:
5 a) one or more of the agents for increasing the activated protein C (APC),
 b) means for detecting at least one of a) cell expression of the agents, and 2) the increased APC in the blood vessel; and
 c) directions for using the kit.

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